PCT

WORLD INTELLECTUAL PROPERTY ORGANIZATION International Bureau



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 7:

C07H 19/10, 19/20, 21/00

(11) International Publication Number:

WO 00/56749

A1

(43) International Publication Date: 28 September 2000 (28.09.00)

(21) International Application Number:

PCT/US00/04032

(22) International Filing Date:

16 February 2000 (16.02.00)

(30) Priority Data:

60/125,867

24 March 1999 (24.03.99)

US

(71) Applicant (for all designated States except US): THE GOV-ERNMENT OF THE UNITED STATES OF AMERICA, represented by THE SECRETARY, DEPARTMENT OF HEALTH AND HUMAN SERVICES [US/US]; National Institutes of Health, Office of Technology Transfer, Suite 325, 6011 Executive Boulevard, Rockville, MD 20852 (US).

(72) Inventors; and

- (75) Inventors/Applicants (for US only): BEAUCAGE, Serge, L. [US/US]; 12905 Beethoven Blvd., Silver Spring, MD 20904 (US). WILK, Andrzej [PL/US]; 3 Pooks Hill Road, Apartment 401, Bethesda, MD 20814 (US). GRAJKOWSKI, Andrzej [PL/US]; 3 Pooks Hill Road, Apartment 816, Bethesda, MD 20814 (US).
- (74) Agents: LARCHER, Carol et al.; Leydig, Voit & Mayer, Ltd., Suite 4900, Two Prudential Plaza, 180 North Stetson, Chicago, IL 60601-6780 (US).

(81) Designated States: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE. LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published

With international search report.

(54) Title: N-ACYLPHOSPHORAMIDITES AND THEIR USE IN OLIGONUCLEOTIDE SYNTHESIS

(57) Abstract

The present invention provides a compound of formula (I), (II), or (III), wherein R¹, R², R², R³, and R³ are the same or different and each is H, an alkyl, an alkenyl, an alkynyl, a cycloalkyl, an aryl, or an aralkyl. Alternatively, either of R² or R^{2'} combined with either of \mathbb{R}^3 or \mathbb{R}^3 comprises a ring. \mathbb{R}^4 is a protecting group or a solid support. \mathbb{R}^5 is H or an alkyl. \mathbb{R}^6 is a protecting group, an amidoalkyl, an alkyl, an alkyl ketone, an alkenyl, an alkynyl, a cycloalkyl, an aryl, or an aralkyl. R15 is H or a protecting group. Q and Q1 are the same or different and each is a nucleoside, an oligonucleotide comprising a nucleoside, or an oligomer comprising a nucleoside, which is of formula (a) or (b), wherein B is a labeling group, an alkyl, an alkenyl, an alkynyl, a cyclic group optionally containing one or more heteroatoms, or an amino; and, E is H, a halogen, a hydroxy, an alkoxy, an ester, an amino or a protecting group. X and X1 are independently O. S. or Se. and n is an integer from 1 to about 300. Each Q in each monomeric unit defined by n can be the same or different. The present invention further provides a method of preparing a polymer using the N-acylphosphoramidite of formula (I) or (II).

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AL	Albania	ES	Spain	LS	Lesotho	SI	Slovenia
AM	Armenia	FI	Finland	LT	Lithuania	SK	Slovakia
AT	Austria	FR	France	LU	Luxembourg	SN	Senegal
ΑU	Australia	GA	Gabon	LV	Latvia	SZ	Swaziland
ΑZ	Azerbaijan	GB	United Kingdom	MC	Мопасо	TD	Chad
BA	Bosnia and Herzegovina	GE	Georgia	MD	Republic of Moldova	TG	Togo
BB	Barbados	GH	Ghana	MG	Madagascar	TJ	Tajikistan
BE	Belgium	GN	Guinea	MK	The former Yugoslav	TM	Turkmenistan .
BF	Burkina Faso	GR	Greece		Republic of Macedonia	TR	Turkey
BG	Bulgaria	HU	Hungary	ML	Mali	TT	Trinidad and Tobago
BJ	Benin	IE	Ireland	MN	Mongolia	UA	Ukraine
BR	Brazil	IL	Israel	MR	Mauritania	UG	Uganda
BY	Belarus	IS	Iceland	MW	Malawi	US	United States of America
CA	Canada .	IT	Italy	MX	Mexico	UZ	Uzbekistan
CF	Central African Republic	JP	Japan	NE	Niger	VN	Viet Nam .
CG	Congo	KE	Kenya .	NL	Netherlands	YU	Yugoslavia
CH	Switzerland	KG	Kyrgyzstan	NO	Norway	ZW	Zimbabwe
CI	Côte d'Ivoire	KP	Democratic People's	NZ	New Zealand		
CM	Cameroon		Republic of Korea	PL	Poland .		
CN	China	KR	Republic of Korea	PT	Portugal		
CU	Cuba	KZ	Kazakstan	RO	Romania		
CZ	Czech Republic	LC	Saint Lucia	RU	Russian Federation		
DE	Germany	LI	Liechtenstein	SD	Sudan		
DK	Denmark	LK	Sri Lanka	SE	Sweden		
EE	Estonia	LR	Liberia	SG	Singapore		